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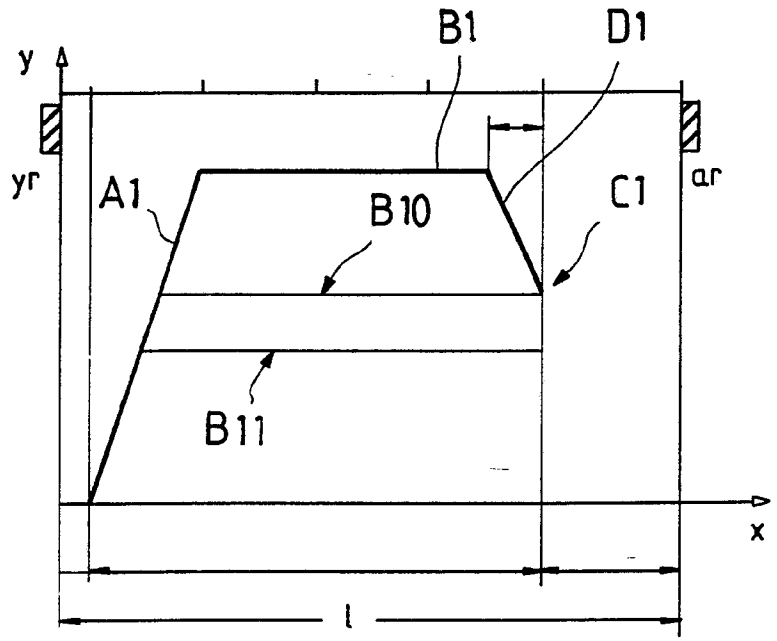

(57) Abstract

A procedure for liquid handling with the aid of a pipette wherein liquid is transferred into the liquid volume of the pipette from a certain starting point of this volume, with substantially linearly accelerated speed (A1), until a desired, predetermined constant speed (B1) has been reached; liquid is transferred at constant speed (B1); the transfer of liquid is abruptly stopped (D1) when the liquid quantity to be transferred has been loaded into the liquid volume; and the liquid quantity is dispensed out from the liquid volume in one or several batches according to the respective steps (A, B, D) presented in the foregoing, so that the liquid transfer steps constitute a closed cycle.

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PROCEDURE FOR HANDLING LIQUID WITH THE AID OF A PIPETTE

The present invention concerns a procedure, as defined in the preamble to claim 1, for liquid handling with the aid of a pipette.

Liquid handling is in this context understood to mean accurate and reproducible transfer, dilution, dispensing, mixing, titration and other manipulation of a desired quantity of liquid. The pipette may be a device with one passage or with multiple passages. In a multi-passage device is for instance provided a plurality of side-by-side, identical devices, which most advantageously can be made to operate simultaneously. In the art a pipette is known which comprises a plunger, a liquid volume and a plunger operating means for transferring a desired quantity of liquid into, and out from, the liquid volume. The operating means usually includes an electric motor with the aid of which the transfer is implemented.

The problem in liquid handling carried out with a pipette is accuracy, speed and reproducibility and, in particular, fitting these together. The liquid quantity to be handled, e.g. in dispensing, is usually small, but it should be handled with a given accuracy and in reproducible manner. On the other hand, the handling of the liquid quantity should be fast in order that the means should be able to process a great number e.g. of samples.

The object of this invention is to eliminate the drawbacks cited in the foregoing. It is particularly an object of the invention, to disclose such a novel procedure for handling predetermined liquid quantities with the aid of a pipette in which predetermined liquid quantities can be handled in a simple and reliable manner, and accurately and offering many possible applications.

The procedure of the invention is characterized by that which is stated in Claim 1.

The procedure of the invention is characterized in that in a first step liquid is transferred into the liquid volume of the pipette with the aid of a plunger from a given starting point in this volume by moving the plunger with a substantially linearly accelerated velocity, until the desired, predetermined constant speed of plunger and liquid has been reached; in a second step the plunger and the liquid are moved at constant speed; in a third step the liquid transfer is abruptly stopped when the liquid quantity that is to be transferred has been loaded into the liquid volume; and the liquid quantity is dispensed in one or several batches out from the liquid volume in accordance with the respective steps just described, so that the liquid transfer steps constitute a closed cycle.

In an embodiment of the invention, deceleration of the plunger movement and of the liquid transfer is commenced with substantially linearly decelerated speed from said constant speed when the liquid quantity already transferred is observed to be close to the ultimate liquid quantity to be transferred.

In an embodiment of the invention, all velocities or speeds, accelerations and decelerations can be set in advance.

In an embodiment of the invention, all velocities or speeds, accelerations and decelerations can be selected in advance from a certain, predetermined set of velocity, speed, acceleration and deceleration values.

In an embodiment of the invention, at dispensing the liquid quantity out from the liquid volume in one or several batches, the last step is a secondary phase in which the liquid volume is emptied past the fixed starting point where the plunger was located at the beginning of the first step.

In an embodiment of the invention, in the secondary phase the liquid volume is emptied by moving the plunger as far as a lower limit, whereafter the liquid volume is returned to the initial state of the first step by moving the plunger to the starting point.

In an embodiment of the invention, at dispensing the liquid quantity out from the liquid volume one goes from the step of constant-speed plunger and liquid movement to a substantially linear deceleration step, which is replaced at the beginning of the secondary phase with a substantially linear acceleration step, and further with a constant speed step, from which one goes, most advantageously, to a substantially linear deceleration step, until the lower limit of the liquid volume is reached, whereafter the plunger is moved from the lower limit of the liquid volume, most advantageously through equivalent steps to the starting point, and the liquid volume is returned to the initial state of the first step, where the process is stopped.

An advantage of the procedure of the invention is exactitude and accuracy of liquid dispensing.

A further advantage of the procedure of the invention is the ease of its modification and its flexibility, whereby it is possible to adapt this procedure to different pipettes, and to single passage as well as multiple passage pipettes.

A further advantage of the procedure of the invention is the versatility of its use in conjunction with any suitable single or multiple passage pipette. Any handling of liquid quantities is managed with ease, whatever the application.

A further advantage of the procedure of the invention is that termination both of the intake phase and of the dispensing phase is implemented abruptly, by arresting the plunger movement e.g. with the aid of an efficient brake means, whereby no residual liquid droplets are incurred on the tip portion of the pipette.

Emptying of the liquid volume, in particular, will therefore take place sharply and accurately, and inaccuracy due to droplets can thus be avoided.

In the following the invention is described in detail, with reference to the attached drawing, wherein:-

Fig. 1 presents, schematically, a pipette;

Fig. 2 presents the kinetic diagram of the pipette plunger and of the liquid transfer, in general form;

Fig. 3 illustrates the basic operation of the pipette with the aid of a kinetic diagram;

Fig. 4 illustrates a dispensing operation implemented with the aid of a pipette, by the aid of a kinetic diagram; and

Fig. 5 illustrates a diluting operation implemented with the aid of a pipette, by the aid of a kinetic diagram.

In Fig. 1 is schematically depicted a pipette comprising a cylinder or liquid volume 1; a plunger 2, fitted into the cylinder volume; a tip part 3; a liquid passage 4 to connect the liquid volume 1 with the tip part; an operating means 5 for moving the plunger 2 in the liquid volume; and a control means 6 for controlling the operating means 5 and by its mediation, the movements of the plunger 2.

In Fig. 2 is depicted the kinetic diagram of the plunger and liquid movement, the x axis representing the longitudinal direction A-A of the liquid volume, and at the same time of the pipette, and where the length of the liquid volume is l. On the y axis of the kinetic diagram is reproduced the velocity with which the plunger is moved, and at the same time the liquid movement speed. It is thus understood that the upper limit and lower limit of the movement of the plunger 2 are separated by the distance l. In the following, the procedure of the invention is generally described, referring to this kinetic diagram.

Liquid is being transferred into the liquid volume 1 of the pipette.

In the first step, liquid is transferred into the liquid volume 1 of the pipette with the aid of the operating means 5 and plunger 2, under control by the control means 6, from a fixed starting point a in this volume by moving the plunger with substantially linearly accelerated velocity A1, until the desired, predetermined constant speed B1 of plunger and liquid has been reached. In the second step, the plunger 2 and the liquid are moved at constant speed B10,B11. In the third step, the liquid transfer is abruptly stopped when the liquid quantity to be transferred has been loaded into the liquid volume C1. The liquid quantity is dispensed from the liquid volume in one or several batches by respective steps like those just described, so that the liquid transfer steps constitute a closed cycle. The whole operation is presented step by step in Fig. 2.

If the constant speed B1 is higher than the fixed constant speed B10, deceleration of the movement of plunger 2 and of the liquid transfer, D1, is commenced with substantially linearly decelerated speed, starting at said constant speed B1, when the liquid quantity already transferred is found to be close to the ultimate liquid quantity to be transferred.

All velocities, speeds, accelerations and decelerations A1, B1, B10, B11, D1 can be preset. These velocities, speeds, accelerations and decelerations are advantageously selectable in advance from a certain set of velocity, speed, acceleration and deceleration values, which can be entered in the memory of the control means.

As Figs 2 and 3 reveal, in the operation of dispensing the liquid quantity from the liquid volume in one (Fig. 2) or several batches (Fig. 3; H, 1-6, W) the last step is a secondary phase T, in which the li-

quid volume is emptied past the fixed starting point a of the plunger 2, the location of the plunger at the beginning of the first step.

In an embodiment of the invention, when the liquid quantity is dispensed out from the liquid volume, one goes from the step of plunger 2 and liquid movement at constant speed B1 to a substantially linear deceleration step D1, which is replaced, at the beginning of the secondary step T, with a substantially linear acceleration step T1 and, further, with a constant speed step T2, from which one goes most advantageously to a substantially linear deceleration step T3, until the lower limit ar of the liquid volume is reached. The plunger 2 is moved from the lower limit ar of the liquid volume 1, through corresponding steps T3,T4, to the starting point a . The liquid volume has been returned to the initial state of the first step, and the process is stopped there. In this case, too, the movement of the plunger 2 back to the starting point is arrested abruptly, T5.

Fig. 5 illustrates, with the aid of a kinetic diagram, a diluting operation implemented with the aid of a pipette. In this instance, reagent is transferred into the liquid volume with the aid of the plunger 2 in an inspiration phase R1, starting at the starting position a , whereafter in a second step I an air bubble is drawn into the liquid volume 1, and thereafter follows the sample inspiration R2. Dispensing takes place similarly as shown in Fig. 3. On the dispensing follows a secondary phase T, as has already been described.

By the procedure of the invention all operating functions of the pipette can be implemented: dispensing, secondary, return to starting position, inspiration and phasing, reagent inspiration air bubble and sample inspiration, hysteresis elimination (see Fig. 4 H), and waste (= w, see Fig. 4).

The invention is not delimited to concern

merely the embodiment example presented in the foregoing: numerous modifications are feasible within the scope of the inventive idea defined by the claims.

CLAIMS

1. A procedure for liquid handling particularly with the aid of a pipette or equivalent device, characterized in that

- liquid is transferred into the liquid volume of the pipette from a certain starting point of this volume, with substantially linearly accelerated speed (A1), until a desired, predetermined constant speed (B1) has been reached;
- liquid is transferred at constant speed (B1);
- the transfer of liquid is abruptly stopped (D1) when the liquid quantity to be transferred has been loaded into the liquid volume;
- the liquid quantity is dispensed out from the liquid volume in one or several batches according to the respective steps (A,B,C) presented in the foregoing, so that the liquid transfer steps constitute a closed cycle.

2. Procedure according to claim 1, characterized in that deceleration of liquid transfer is commenced with substantially linearly decelerated speed (C1) from said constant speed (B1) when the liquid quantity already transferred is found to be close to the ultimate liquid quantity to be transferred.

3. Procedure according to claim 1 or 2, characterized in that all velocities, speeds, accelerations and decelerations can be set in advance.

4. Procedure according to claim 3, characterized in that all velocities, speeds, accelerations and decelerations are selectable in advance from a certain, predetermined set of velocity, speed, acceleration and deceleration values.

5. Procedure according to any one of the preceding claims, characterized in that when the liquid quantity is being dispensed out from the liquid volume in one or several batches, the last step is a secondary

phase in which the liquid volume is emptied past the fixed starting point.

6. Procedure according to claim 5, characterized in that in the secondary phase the liquid volume is emptied to the lower limit, whereafter return to the starting point of the liquid volume is effected.

7. Procedure according to claim 6, characterized in that when the liquid quantity is being dispensed out from the liquid volume, one goes from the constant speed step to a substantially linear deceleration step, which is replaced, at the beginning of the secondary phase, with a substantially linear acceleration step, and further with a constant speed step, from which one goes most advantageously to a substantially linear deceleration step, until the lower limit of the liquid volume is reached, whereafter transition is made from the lower limit of the liquid volume, most advantageously through corresponding steps, to the starting point of the liquid volume, where the process is stopped.

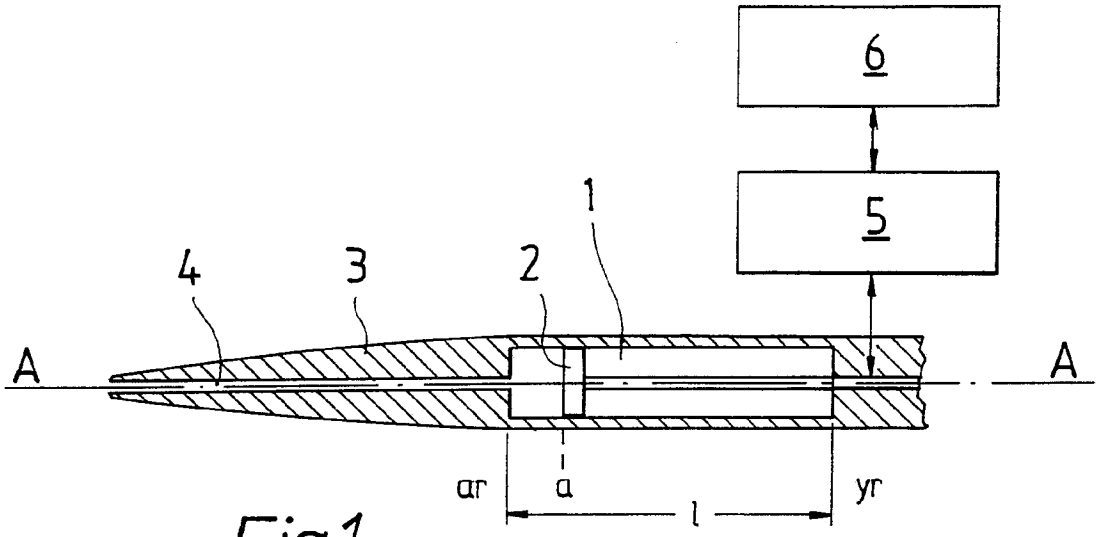

Fig.1

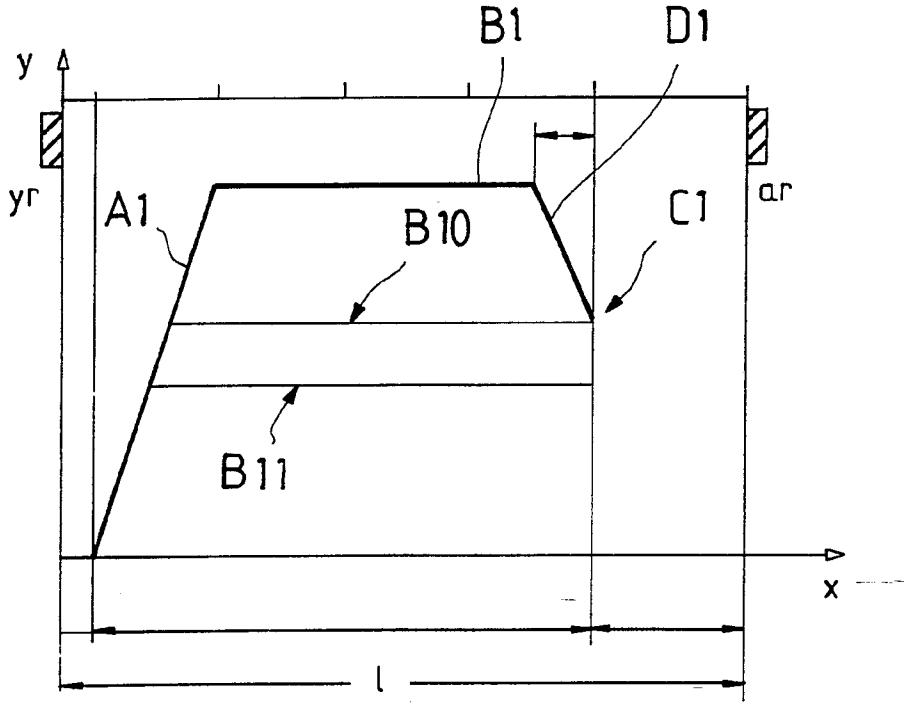

Fig.2

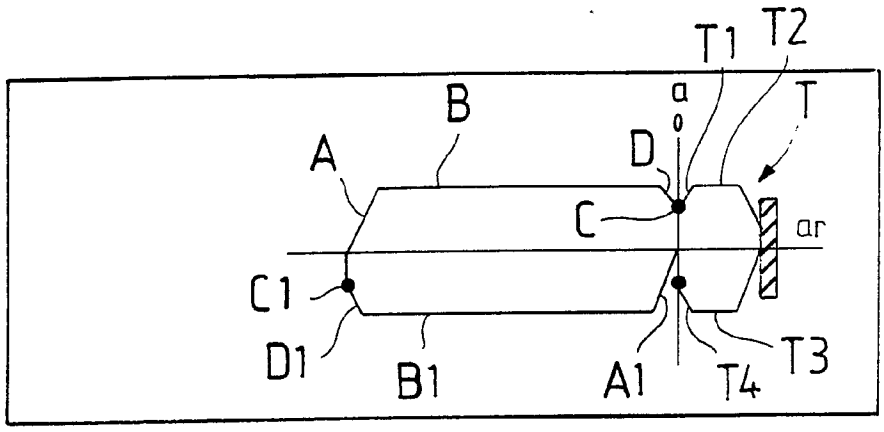

Fig.3

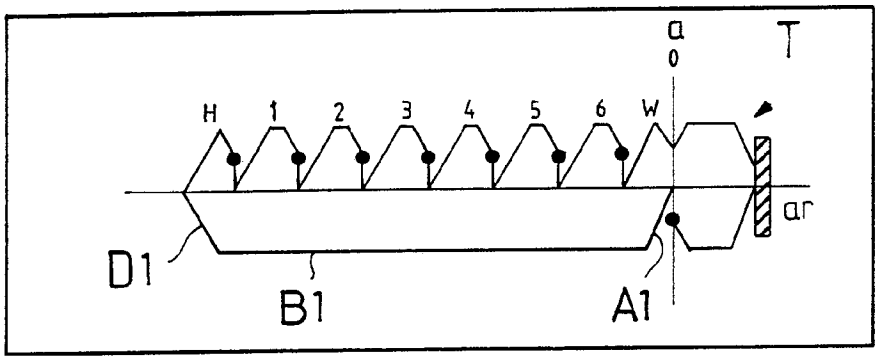

Fig.4

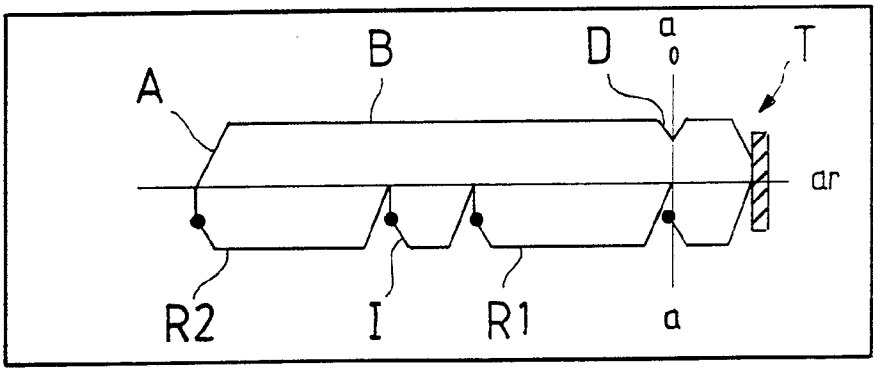

Fig.5

INTERNATIONAL SEARCH REPORT

International Application No PCT/FI 91/00136

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC5: B 01 L 3/02

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
IPC5	B 01 L; G 01 N; G 01 F

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in Fields Searched[8]

SE,DK,FI,NO classes as above

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category *	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
A	SE, B, 385090 (O A SUOVANIEMI) 8 June 1976, see page 2, line 38 - page 3, line 14; claim 3 -- --------	1-7

* Special categories of cited documents: [10]

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
9th August 1991	1
International Searching Authority	**Signature of Authorized Officer**
SWEDISH PATENT OFFICE	Gunnel Wästerlid

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ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.PCT/FI 91/00136

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the Swedish Patent Office EDP file on 91-06-27
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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
SE-B- 385090	76-06-08	DE-A-	2229623	72-12-28
		FR-A-B-	2143490	73-02-02
		GB-A-	1395424	75-05-29
		US-A-	3810391	74-05-14